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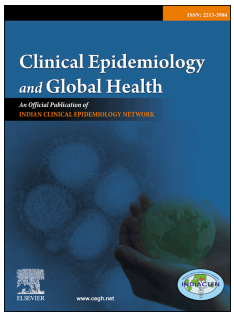

Acceptance of COVID-19 vaccination and correlated variables among global populations: A systematic review and meta-analysis

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PII: S2213-3984(21)00207-4

DOI: https://doi.org/10.1016/j.cegh.2021.100899

Reference: CEGH 100899

To appear in: *Clinical Epidemiology and Global Health*

Received Date: 2 April 2021

Revised Date: 28 June 2021

Accepted Date: 28 October 2021

Please cite this article as: Nindrea RD, Usman E, Katar Y, Sari NP, Acceptance of COVID-19 vaccination and correlated variables among global populations: A systematic review and meta-analysis, *Clinical Epidemiology and Global Health* (2021), doi: https://doi.org/10.1016/j.cegh.2021.100899.

Original Article

Title:

Acceptance of COVID-19 Vaccination and Correlated Variables among Global Populations: A Systematic Review and Meta-Analysis

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Running title:

Acceptance of COVID-19 Vaccination and Correlated Variables among Global Populations

Total word count: 3,813

Total number of references: 45

Number of Tables: 2

Number of Figures: 5

Original Article

Acceptance of COVID-19 Vaccination and Correlated Variables among Global Populations: A Systematic Review and Meta-Analysis

Abstract

Introduction: The most awaited solution is an efficient COVID-19 vaccine. COVID-19 vaccine acceptance has not been studied in a meta-analysis. The objective of this research was to find the acceptance of COVID-19 vaccination and correlated variables.

Methods: A systematic review of studies on acceptance of COVID-19 vaccination and correlated variables in the ProQuest, PubMed, and EBSCO to find relevant articles published between January 2020 and March 2021. Using fixed and random-effect models, the risk factors Pooled Odds Ratio (POR) were measured. The heterogeneity was calculated using the I-squared formula. Egger's and Begg's tests were utilised to determine publication bias. STATA 16.0 was used for all data processing and analysis.

Results: This study results showed the related factors for COVID-19 vaccination acceptance, high income has the highest odd ratio (POR=2.36), followed by encountered with COVID-19 (POR=2.34), fear about COVID-19 (POR=2.07), perceived benefits (POR=1.81), flu vaccine during the previous season (OR=1.69), healtcare workers (POR=1.62), male (POR=1.61), married (POR=1.59), perceived risk (POR=1.52), trust in health system (POR=1.52), chronic diseases (POR=1.47), high education (POR=1.46), high level of knowledge (POR=1.39), female (1.39), and older age (POR=1.07). The heterogeneity calculation showed homogenous among studies in high income, fear about COVID-19, healthcare workers, married, chronic diseases, and female ($I^2 \leq 50\%$). For the studies included in this review, there was no apparent publication bias.

Conclusion: The analysis of this review may be useful to the nation in determining the best method for implementing COVID-19 mass vaccination programs based on relevant factors that influence vaccine acceptance.

Keywords: Acceptance; COVID-19; Risk Factors; Vaccine

1. Introduction

Since 2020, COVID-19 widespread has become a serious community health concern. The COVID-19 emergency afflicted many nations. By March 2021, there had been over 128.2 million confirmed cases of the disease, with 2.8 million deaths.[1]

COVID-19 not only has a major health effect, but it also has a significant economic impact that should not be ignored. It has resulted in a major decline in workforces and an increase in jobless around the world.[2] These negative consequences have prompted pharmaceutical firms to produce a vaccine as soon as possible. At the end of 2020, multiple vaccines to prevent COVID-19 infection were approved. and there were more than fifty COVID-19 vaccine potential in production.[3] Vaccination programs have started in a number of countries around the world.[4] Despite this, people continue to have concerns about vaccine safety and effectiveness, including the durability of COVID-19 defense, as many cases of reinfection have been documented.[5,6] Furthermore, the rapid production of vaccines raises concerns about their efficacy. Vaccine production has historically been connected to harmful effects.[7]

For decades, vaccines have proven to be an effective means of disease prevention.[8] Vaccine hesitancy and refusal, on the other hand, are major issues around the world, causing the World Health Organization (WHO) to name this confusion as one of the top ten health risks for 2019.[9] Vaccine apprehension has been linked to religious values, personal opinions, and safety issues based on widespread misconceptions, such as the connection between vaccines and autism, brain injury, and other disorders, according to various reports.[10] Regrettably,

there have been inadequate research undertaken in order to determine the global population's attitudes toward vaccination. No previously published work has been analyzed by meta-analysis to our knowledge. The findings of this study may help the government figure out the important way to execute COVID-19 mass vaccination programs.

2. Materials and Methods

2.1. Study design and research sample

To assess current articles related to the acceptance of COVID-19 vaccination and correlated variables, a systematic review and meta-analysis studies were conducted. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline was followed in this study.[11] There are three databases, i.e. ProQuest, PubMed, and EBSCO were used to search for relevant articles published between January 2020 and March 2021. In this research, the acceptance of COVID-19 vaccine was the dependent variable. The independent variables were the determinant factors of COVID-19 vaccine acceptance.

2.2 Research procedure

The keywords used to search related articles in ProQuest, PubMed, and EBSCO between January 2020 and March 2021 were: COVID-19 OR Coronavirus AND Vaccine AND Acceptance. The included articles limited to original or research articles, with English texts and with human as study subjects. The inclusion criteria included study on the acceptance of COVID-19 vaccine and related factors with study design of cross sectional. The study exclusion criteria included full text version is unavailable, unrelated topics or subjects, and data in publications that could not be extracted or used for further review. The Newcastle-Ottawa Quality Assessment Scale (NOS) modified for cross-sectional study was used to evaluate the articles' quality. 0-3, 4-6, and 7-9 were used to categorize articles into poor,

medium, and high quality categories.[12] The PRISMA flowcharts were used to illustrate the steps involved in finding research articles (Figure 1).

2.3 Data analysis

For further data analysis, the Pooled Odds Ratio (POR) of the effect size of each risk factor from the derived data was determined with a confidence degree of 95 percent. The heterogeneity was calculated using the I^2 formula, and $I^2 > 50\%$ indicated that there was heterogeneity between studies. If the result was heterogeneous, the random effect model was used, and if the result was homogeneous, the fixed effect model was used. Furthermore, the findings were viewed as forest plots, and publication bias was assessed using Egger's and Begg's tests. The $p > 0.05$ results from the two tests revealed that there was no publication bias among the studies. For lower middle income countries (LMICs), restricted-maximum likelihood random effects meta-regression was used to examine the role of covariate. STATA 16.0 was used for all data processing and analysis.

3. Results

This systematic review study included 24 recent studies conducted to the acceptance of COVID-19 vaccination and related factors (Table 1). The total sample from the included studies was 56,913 participants.[13-36]

Table 1 is based on a synthesis of studies correlated variables for acceptance of COVID-19 vaccination, including 24 cross sectional studies. This study found factors contributing to acceptance of COVID-19 vaccination included older age, male, female, married, high education, high income, healthcare workers, chronic diseases, high level of knowledge, perceived risk, perceived benefits, fear about COVID-19, encountered with COVID-19, flu vaccine during the previous season and trust in health system.

Meta-estimate of COVID-19 vaccination acceptance and correlated variables among global populations (Table 2 and Figure 2). Table 2 and Figure 2 showed high income has the highest Pooled Odds Ratio (POR, 95% CI) (2.36, 1.94-2.87), followed by encountered with COVID-19 (2.34, 1.98-2.76), fear about COVID-19 (2.07, 1.79-2.39), perceived benefits (1.81, 1.61-2.00), flu vaccine during the previous season (1.69, 1.57-1.82), healthcare workers (1.62, 1.42-1.85), male (1.61, 1.47-1.78), married (1.59, 1.38-1.83), perceived risk (1.52, 1.43-1.62), trust in health system (1.52, 1.44-1.61), chronic diseases (1.47, 1.31-1.65]), and high education (1.46, 1.34-1.59), high level of knowledge (1.39, 1.29-1.49), female (1.39, 1.19-1.61]), and older age (1.07, 1.05-1.10) with COVID-19 vaccination acceptance. The heterogeneity calculation showed homogenous among studies in high income, fear about COVID-19, healthcare workers, married, chronic diseases, and female ($I^2 \leq 50\%$).

The results of Egger's and Begg's test to assess bias among studies included (Table 3). Table 3 showed that based on Egger's and Begg's test result ($p > 0.05$), related factors of older age, male, female, married, high education, high income, healthcare workers, chronic diseases, high level of knowledge, perceived risk, perceived benefits, fear about COVID-19, encountered with COVID-19, flu vaccine during the previous season and trust in health system had no publication bias among studies combined.

The association between LMICs and COVID-19 vaccine acceptance based on meta-regression (Figure 3). Figure 3 showed that the association between LMICs and decreased COVID-19 vaccine acceptance ($p=0.02$). This analysis confirmed the COVID-19 vaccine acceptance may vary across these country types.

4. Discussion

Our results found high income had high acceptance of COVID-19 vaccination. The acceptance rate rises with economic status. A study highlighted the importance of community

confidence in vaccine uptake and found a scarcity of studies in low and middle-income households on vaccine uptake based on community trust.[37] A higher willingness to receive COVID-19 vaccination was correlated with a higher income level, likely due to better access to high-quality information, such as through better television channels and/or through communication with people living abroad in COVID-19-affected countries, and/or because such people tend to live in towns where the virus is more prevalent.[15]

Encountered with COVID-19, fear of COVID-19 and perceived risk have found to be positively correlated with vaccine acceptance in this study. Previous studies in Asia have shown that a positive attitude toward vaccination is linked to a perception of risk or fear about COVID-19.[38-40] Another study showed that a high perceived risk was related to COVID-19 vaccine acceptance among Saudi Arabian community members and Congo healthcare staff.[26,31] As a consequence, it is crucial to boost community expectations of risk. Low risk perception can be linked to vaccine acceptance, as well as social distancing and other community health defensive measures. These associations may be complicated; for example, a person who practices social distancing strategies can believe their risk is low but still wants to get vaccinated.

Vaccination intention is strongly influenced by perceived benefits. Perceived advantages have been found to be determinant factors in some studies.[21,25] In the context of vaccination, perceived benefits are characterized as a person's attitudes toward vaccination. It's important to have public health intervention programs that concentrate on changing people's perceptions of vaccination's benefits while also removing the obstacles that have been identified.

According to the findings of this report, there is a correlation between influenza vaccination during the past season and COVID-19 vaccination acceptance. Related positively flu vaccination during the past season to COVID-19 vaccine acceptance.[24,30] COVID-19 and seasonal influenza are likely to co-circulate during the winter of 2020-2021. Healthcare staff

in France are advised to get vaccinated for the flu season. Patients with concomitant flu and COVID-19 can have poorer outcomes than patients with COVID-19 alone, so lowering the risk of coinfections in susceptible patients is important.

Healthcare staff were more enthusiastic about a COVID-19 vaccine than non-healthcare staff, according to our results. In previous research, self-protection and a willingness to protect families, friends, and patients were the driving factors behind healthcare staff getting vaccinated.[41,42] Since healthcare staff have a more in-depth understanding of COVID-19, they will be more likely to protect themselves and not spread the virus to their family members. As a result, they could be more likely to consider the vaccine than those who work in non-medical fields.

Sex and married were also found to be positively correlated with vaccine acceptance in this study. Previous studies have shown that men, women, and married people are more likely to support immediate pandemic vaccination.[17,24,27] This may be due to everyone at risk in the gender group and marital status. Older people agreed to be vaccinated in our report. This may be because the belief that older adults and people with severe comorbidities or chronic diseases are more vulnerable to COVID-19's negative effects can cause a lot of anxiety among the elderly.[43]

Individuals with university/higher levels of education recorded having a substantially higher level of knowledge about COVID-19 vaccine acceptance. Related scenarios were observed in previous studies, showing that people with a higher educational experience learned more about COVID-19.[13,35] It's likely that more informed people are more aware of and caring about their health and well-being as a result of improved access to more media sources, as well as becoming more interested in life activities that may affect them.

Participants' confidence in the health-care system was discovered to be a major indicator of their ability to use the COVID-19 vaccine. In response to the present situation, a low

confidence in the health system could put community health at risk. The application of preventive health services like vaccination has been linked to a higher level of confidence in the health system.[44,45]

This meta-analysis study has a number of limitations. Four articles seemed to be suitable for inclusion in this meta-analysis, but they lacked adequate evidence and had results that were insignificant for data estimation. This problem will exacerbate the risk of selection bias.

The results show that health departments should implement urgent health promotion services and disseminate more reliable information. Governments should take action to ensure that people have enough information, have healthy attitudes, and have positive opinions about COVID-19 vaccines.

5. Conclusion

This study results showed the related factors for COVID-19 vaccination acceptance, high income has the highest odd ratio, followed by encountered with COVID-19, fear about COVID-19, perceived benefits, flu vaccine during the previous season, healtcare workers, male, married, perceived risk, trust in health system, chronic diseases, high education, high level of knowledge, female, and older age. The heterogeneity calculation showed homogenous among studies in low income, fear about COVID-19, healthcare workers, married, chronic diseases, and female. The findings of this study may help the government figure out the best way to implement COVID-19 mass vaccination programs.

Funding/ Financial Support

This study obtained no particular support from public, private, or non-profit funding agencies.

Acknowledgments

The authors would like to express their gratitude to Riyani Betri Novialita, MA, for her assistance in data collection.

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Legends

Figure 1. The PRISMA flowcharts

Figure 2. Forest plots of COVID-19 vaccination acceptance and correlated variables among global populations

Figure 3. The association between LMICs and COVID-19 vaccine acceptance based on meta-regression

Table 1. Systematic review of COVID-19 vaccination acceptance and correlated variables among global populations

Table 2. Meta-estimate of COVID-19 vaccination acceptance and correlated variables among global populations

Table 3. The results of Egger's and Begg's test to assess bias among studies included

Table 1. Systematic review of COVID-19 vaccination acceptance and correlated variables among global populations

First author, year	Year of study	Region	Study design	Total samples	Determinant factors (OR, 95% CI)	NOS
Al-Qerem et al[13]	2021	Middle Eastern	Cross sectional	1,144	Older age (2.42, 1.22-4.79) High level of knowledge (1.50, 1.38-1.62)	7
Caserotti et al[14]	2021	Italy	Cross sectional	2,267	Perceived risk (4.86, 3.53-6.74) Older age (1.47, 1.14-1.89)	7
Ditekemena et al[15]	2021	Republic of Congo	Cross sectional	4,131	High income (2.31, 1.85-2.88) High education (1.82, 1.55-2.13) Perceived risk (7.78, 5.75-10.53) Chronic disease (1.26, 1.04-1.53)	6
Seale et al[16]	2021	Australia	Cross sectional	1,420	Female (1.40, 1.10-1.80) Older age (3.10, 1.80-5.30) Chronic disease (1.40, 1.10-2.0)	7
Sallam et al[17]	2021	Jordan, Kuwait, Saudi Arabia	Cross sectional (online questionnaire)	3,414	Male (1.54, 1.28-1.85) Chronic disease (1.55, 1.15-2.09)	7
Qattan et al[18]	2021	Saudi Arabia	Cross sectional	736	Older age (2.22, 0.96-5.17) Male (1.61, 0.97-2.67)	7
Saied et al[19]	2021	Egypt	Cross sectional	2,133	Healthcare workers (2.26, 1.34-3.81)	7
Alley et al[20]	2021	Australia	Cross sectional	2,343	Female (1.89, 1.20-2.97) Chronic disease (1.39, 0.98-1.97)	7
Wong et al[21]	2021	Hongkong	A population-based survey	1,200	Older age (2.03, 1.48-2.77) Chronic disease (1.89, 1.50-2.38) Perceived risk (1.09, 1.00-1.17) Perceived benefits of vaccination (1.79, 1.59-1.99) Trust in health system (1.36, 1.25-1.48)	7
Alqudeimat	2021	Kuwait	Cross	2,368	Encountered with confirmed	6

et al[22]			sectional		COVID-19 (5.67, 4.14-7.77) Flu vaccine during the previous season (1.35, 1.24-1.47)	
Gagneux-Brunon et al et al[23]	2021	French	Cross sectional	1,554	Male (2.21, 1.69-2.90) Older age (3.45, 1.53-7.77) Flu vaccine during the previous season (7.22, 5.68-9.19) Fear about COVID-19 (2.03, 1.58-2.61) Perceived risk (2.09, 1.70-2.57)	6
Wang et al (a)[24]	2021	Hongkong	Cross sectional	2,047	Married (1.69, 1.33-2.14) Flu vaccine during the previous season (2.25, 1.74-2.93)	7
Verger et al[25]	2021	France	Cross sectional	2,678	Female (1.22, 0.96-1.55) Perceived risk (3.01, 2.38-3.79) Perceived benefits of vaccination (1.57, 1.05-2.36)	5
Nzaji et al[26]	2020	Republic of Congo	Cross sectional	613	Married (1.25, 0.85-1.83) Healtcare workers (1.92, 1.31-2.81) Encountered with confirmed COVID-19 (8.83, 1.18-66.04)	7
Lazarus et al[27]	2020	Global (19 countries)	Cross sectional	13,426	Older age (1.73, 1.48-2.02) High education (1.34, 1.21-1.48) Trust in health system (1.67, 1.54-1.80)	5
Detoc et al[28]	2020	France	Cross sectional (online survey)	3,259	Male (1.71, 1.42-2.06) Older age (2.25, 1.76-2.87) Healthcare workers (1.57, 1.33-1.86) Fear about COVID-19 (2.09, 1.75-2.49) Perceived risk (1.83, 1.54-2.16)	6
Bell et al[29]	2020	England	Cross sectional	1,252	High income (2.53, 1.67-3.83)	6
Wang et al (b)[30]	2020	Hongkong, China	Cross sectional	806	Male (2.78, 1.69-4.58) Encountered with confirmed COVID-19 (1.63, 1.14-2.33) Flu vaccine during the previous	7

					season (2.03, 1.47-2.81)	
Al-Mohaithef et al[31]	2020	Saudi Arabia	Cross sectional (web survey)	992	Married (1.57, 1.20-2.06) Perceived risk (2.48, 1.11-3.95) Trust in the health system (2.85, 1.03-4.80)	7
Harapan et al[32]	2020	Indonesia	Cross sectional	1,359	Female (1.55, 1.01-2.38) Older age (2.10, 1.04-4.23) Healthcare workers (1.43, 1.06-1.93)	7
Lin et al[33]	2020	China	Cross sectional	3,541	Perceived benefits of vaccination (3.14, 2.05-4.83) Encountered with confirmed COVID-19 (1.65, 1.31-2.09)	7
Malik et al[34]	2020	U.S	Cross sectional	672	Older age (1.81, 0.99-3.29)	5
Sherman et al[35]	2020	UK	Cross sectional	1,500	Older age(1.04, 0.99-1.04) Perceived risk (1.03, 0.85-1.81) High level of knowledge (1.08, 1.04-1.39)	7
Wang et al (c)[36]	2020	China	Cross sectional	2,058	Male (1.25, 1.03-1.52) Married (1.70, 1.26-2.29) Perceived benefits of vaccination (1.56, 1.08-2.25)	5
Total samples				**56,913**		

Abbreviation: CI= confidence interval; HR= hazard ratio; OR= odds ratio; NOS, Newcastle–Ottawa Quality Assessment Scale

Table 2. Meta-estimate of COVID-19 vaccination acceptance and correlated variables among global populations

Related factors	First author	OR (95% CI)	POR (95% CI)	Heterogeneity	
				I^2 (%)	p
Older Age			**1.07 (1.05-1.10)**	**92.7**	**<0.001**
	Al-Qerem et al[13]	2.42 (1.22-4.79)			
	Caserotti et al[14]	1.47 (1.14-1.89)			
	Seale et al[16]	3.10 (1.80-5.30)			
	Qattan et al[18]	2.22 (0.96-5.17)			
	Wong et al[21]	2.03 (1.48-2.77)			
	Gagneux- Brunon et al[23]	3.45 (1.53-7.77)			
	Lazarus et al[27]	1.73 (1.48-2.02)			
	Detoc et al[28]	2.25 (1.76-2.87)			
	Harapan et al[32]	2.10 (1.04-4.23)			
	Malik et al[34]	1.81 (0.99-3.29)			
	Sherman et al[35]	1.04 (0.99-1.04)			
Male			**1.61 (1.47-1.78)**	**70.6**	**0.004**
	Sallam et al[17]	1.54 (1.28-1.85)			
	Qattan et al[18]	1.61 (0.97-2.67)			
	Gagneux- Brunon et al[23]	2.21 (1.69-2.90)			
	Detoc et al[28]	1.71 (1.42-2.06)			
	Wang et al (b)[30]	2.78 (1.69-4.58)			
	Wang et al (c)[36]	1.25 (1.03-1.52)			
Female			**1.39 (1.19-1.61)**	**5.0**	**0.358**
	Seale et al[16]	1.40 (1.10-1.80)			
	Alley et al[20]	1.89 (1.20-2.97)			
	Verger et al[25]	1.22 (0.96-1.55)			
	Harapan et al[32]	1.55 (1.01-2.38)			
Married			**1.59 (1.38-1.83)**	**0**	**0.579**
	Wang et al (a)[24]	1.69 (1.33-2.14)			
	Nzaji et al[26]	1.25 (0.85-1.83)			
	Al-Mohaithef et al[31]	1.57 (1.20-2.06)			

	Wang et al (c)[36]	1.70 (1.26-2.29)			
High education			**1.46 (1.34-1.59)**	**90.2**	**0.001**
	Ditekemena et al[15]	1.82 (1.55-2.13)			
	Lazarus et al[27]	1.34 (1.21-1.48)			
High income			**2.36 (1.94-2.87)**	**0**	**0.705**
	Ditekemena et al[15]	2.31 (1.85-2.88)			
	Bell et al[29]	2.53 (1.67-3.83)			
Healthcare workers			**1.62 (1.42-1.85)**	**3.9**	**0.373**
	Saied et al[19]	2.26 (1.34-3.81)			
	Nzaji et al[26]	1.92 (1.31-2.81)			
	Detoc et al[28]	1.57 (1.33-1.86)			
	Harapan et al[32]	1.43 (1.06-1.93)			
Chronic disease			**1.47 (1.31-1.65)**	**45.4**	**0.120**
	Ditekemena et al[15]	1.26 (1.04-1.53)			
	Seale et al[16]	1.40 (1.10-2.000			
	Sallam et al[17]	1.55 (1.15-2.09)			
	Alley et al[20]	1.39 (0.98-1.97)			
	Wong et al[21]	1.89 (1.50-2.38)			
High level of knowledge			**1.39 (1.29-1.49)**	**93.4**	**<0.001**
	Al-Qerem et al[13]	1.50 (1.38-1.62)			
	Sherman et al[35]	1.08 (1.04-1.39)			
Perceived risk			**1.52 (1.43-1.62)**	**97.5**	**<0.001**
	Caserotti et al[14]	4.86 (3.53-6.74)			
	Ditekemena et al[15]	7.78 (5.75-10.53)			
	Wong et al[21]	1.09 (1.00-1.17)			
	Gagneux- Brunon et al[23]	2.09 (1.70-2.57)			
	Verger et al[25]	3.01 (2.38-3.79)			
	Detoc et al[28]	1.83 (1.54-2.16)			

	Al-Mohaithef et al[31]	2.48 (1.11-3.95)			
	Sherman et al[35]	1.03 (0.85-1.81)			
Perceived benefits			**1.81 (1.64-2.00)**	**59.9**	**0.058**
	Wong et al[21]	1.79 (1.59-1.99)			
	Verger et al[25]	1.57 (1.05-2.36)			
	Lin et al[33]	3.14 (2.05-4.83)			
	Wang et al (c)[36]	1.56 (1.08-2.25)			
Fear about COVID-19			**2.07 (1.79-2.39)**	**0**	**0.852**
	Gagneux- Brunon et al[23]	2.03 (1.58-2.61)			
	Detoc et al[28]	2.09 (1.75-2.49)			
Encountered with COVID-19			**2.34 (1.98-2.76)**	**93.3**	**<0.001**
	Alqudeimat et al[22]	5.67 (4.14-7.77)			
	Nzaji et al[26]	8.83 (1.18-66.04)			
	Wang et al (b)[30]	1.63 (1.14-2.33)			
	Lin et al [33]	1.65 (1.31-2.09)			
Flu vaccine during the previous season			**1.69 (1.57-1.82)**	**98.3**	**<0.001**
	Alqudeimat et al[22]	1.35 (1.24-1.47)			
	Gagneux- Brunon et al[23]	7.22 (5.68-9.19)			
	Wang et al (a)[24]	2.25 (1.74-2.93)			
	Wang et al (b)[30]	2.03 (1.47-2.81)			
Trust in health system			**1.52 (1.44-1.61)**	**86.5**	**0.001**
	Wong et al[21]	1.36 (1.25-1.48)			
	Lazarus et al[27]	1.67 (1.54-1.80)			
	Al-Mohaithef et al[31]	2.85 (1.03-4.80)			

Abbreviation: CI= confidence interval; OR= odds ratio; POR= Pooled odds ratio; I^2> 50%, heterogeneity

Table 3. The results of Egger's and Begg's test to assess bias among studies included

Related factors	Study bias	
	Egger's test	**Begg's test**
Older age	0.925	0.139
Male	0.269	0.573
Female	0.137	0.052
Married	0.159	0.174
High education	0.112	0.317
Low income	0.115	0.317
Healthcare workers	0.304	0.174
Chronic diseases	0.804	1.000
High level of knowledge	0.811	0.317
Perceived risk	0.577	0.458
Perceived benefits	0.740	0.497
Fear about COVID-19	0.160	0.227
Encountered with COVID-19	0.051	0.174
Flu vaccine during the previous season	0.280	1.000
Trust in health system	0.767	0.602

$p>0.05$, no publication bias.